PCN18

INTERMITTENT VERSUS CONTINUOUS CHEMOTHERAPY FOR FIRST-LINE TREATMENT OF UNRESECTABLE METASTATIC COLORECTAL CANCER (CCRM): SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: To perform a systematic review and meta-analysis of all randomized controlled trials comparing efficacy of Intermittent versus continuous chemotherapy (CT) for first-line treatment of unresectable Metastatic Colorectal Cancer (CCRm). **METHODS:** Several databases were searched, including MEDLINE, EMBASE, LILACS, and CENTRAL. The primary endpoint was overall survival (OS). The data extracted from the studies were combined by using Hazard Ratio (HR) with their corresponding 95% confidence intervals (CI95%). **RESULTS:** Overall, 733 references were identified and screened. The final analysis included 4 trials comprising 1,827 patients analyzed. There was no statistically significant difference between the groups (Intermittent vs continuous chemotherapy) on the analysis of overall survival (fixed effect: HR=1.03, CI95%=0.92 to 1.16; p=0.56). No heterogeneity was detected on this analysis (Chi2 = 2.88, df = 3 (P=0.41); I2 = 0%). **CONCLUSIONS:** Overall survival was similar between groups. The intermittent chemotherapy regimen provides better quality of life that the scheme is continued and probably cost saving.

PCN19

THE BROADER BURDEN OF HPV-RELATED DISEASE IN ENGLAND: A PRELIMINARY ANALYSIS

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OBJECTIVES: The Human Papillomavirus (HPV) is a known cause of cervical cancer and genital warts, and causes a proportion of vaginal, vulval, penile, anal, and head and neck (H+N) cancers. Quantifying the broader burden of HPV-related cancers is important as this group represents approximately 5.2% of all cancers. **METHODS:** Using cancer registry data covering the population of England (2003-2008), we examined incidence of HPV-related cancers. HPV-associated sites were identified (cervix, vulva, vagina, anus, penis and H+N) and grouped according to ICD-O-3 site. Incidence rates were age-adjusted (ASR) to the European standard population by the direct method and 95% Confidence intervals (95% CI) calculated using STATA SE11.0. A literature review was conducted to ascertain the percentage attributable to HPV for each cancer type. Over 300 articles were reviewed and graded by relevance, sample size, and date. **RESULTS:** ASRs for HPV-related cancers were: vagina/vulval cancers: 0.33(95% CI 0.3-0.4) and 1.4(95% CI: 1.3-1.4) per 100,000 females. Penile cancer: 0.8(95% CI: 0.7-0.8) per 100,000 males. Anal cancers: 10.8(95% CI:10.7-11.1) males and 6.0(95% CI:5.8-6.0) females per 100,000. Base of tongue and lingual tonsil: 0.06(95% CI:0.06-0.07) males and 0.02(95% CI:0.01-0.02) females per 100,000; tonsil: 0.11(95% CI:0.10-0.12) males and 0.03(95% CI:0.03-0.04) females per 100,000; oropharynx: 0.05(95% CI:0.05-0.06) males and 0.02(95% CI:0.01-0.02) females per 100,000. Estimates reported in literature for percentage of HPV-attributable cases ranged from 70-100% for cervical, 27-76% vulval, 70-90% vaginal, 40-54% penile, 76-90% anal, and 11-72% for HPV-associated H+N cancers. The most commonly reported strains were HPV 16, 18, 31, and 33. **CONCLUSIONS:** The incidence of HPV-related cancers represents a significant burden. Recent incidence estimates are similar to 2002 estimates, apart from an increase in anal cancers. Estimates of the HPV-attributable percentage for each cancer and projected prevalence will be used to assess the impact of implementing a quadrivalent HPV vaccination programme in England.

PCN20

SYSTEMATIC REVIEW OF SKELETAL RELATED EVENTS IN BREAST CANCER

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OBJECTIVES: Metastatic bone lesions lead to an increase in the risk for skeletal related events (SREs), including pathologic fracture, spinal cord compression, hypercalcemia of malignancy, and severe bone pain requiring palliative radiotherapy or surgery to bone. Twenty-nine percent of breast cancer patients with bone metastases develop SREs. Our objective was to systematically review the literature on the impact of SREs on pain, quality of life (QOL), morbidity, survival and cost in breast cancer patients. **METHODS:** We searched PubMed, limiting to peer-reviewed English-language human studies published in 2000-2010. The search was based on a SRE definition accepted by the U.S. Food and Drug Administration and European Medicines Agency. Articles were included if they were randomized-controlled trials, clinical trials with appropriate control group, systematic reviews, meta-analyses, case-series or economic analyses, and were excluded if they did not provide interpretable results on outcomes of interest. **RESULTS:** A total of 209 articles were screened, of which 131 were excluded, and 78 were abstracted. No studies, outside of bisphosphonate trials, were identified that examined the impact of SREs as a group on clinical outcomes. Bisphosphonate treatment reduced SREs, and hence improved pain and QOL. Literature indicated that presence of pathologic bone fractures is correlated with increased risk of death. Spinal cord compression significantly impaired ambulatory function and shortened survival of these patients compared to historical controls. Radiation therapy improved pain and QOL while bone surgery was shown to improve pain and function with vertebrectomy. Limited evidence suggested treatment cost of SREs is $14,000 (95% CI: $11,000-$17,000) per patient. **CONCLUSIONS:** Presence of clinical SREs is associated with worse morbidity and survival, while their treatment is associated with improved pain, QOL and morbidity among breast cancer patients. SREs appear to increase cost of treatment substantially.

PCN21

SYSTEMATIC REVIEW OF SKELETAL RELATED EVENTS IN PROSTATE CANCER

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OBJECTIVES: Between 65-75% of patients with prostate cancer experience metastatic bone disease. Metastatic bone lesions increase risk for skeletal related events (SREs), which include clinical SREs (pathologic fracture, spinal cord compression, hypercalcemia of malignancy) and treatments of clinical SREs (radiotherapy or surgery to bone) resulting from severe bone pain. Our objective was to systematically review the literature on the impact of SREs on pain, quality of life (QOL), morbidity, survival and cost in prostate cancer patients. **METHODS:** We searched PubMed, limiting to peer-reviewed English-language human studies published in 2000-2010. The search was based on SRE definition accepted by the US Food and Drug Administration and European Medicines Agency. Articles were included if they were randomized-controlled trials, clinical trials with appropriate control group, systematic reviews, meta-analyses, case-series or economic analyses, and were excluded if they did not provide interpretable results on outcomes of interest. **RESULTS:** A total of 209 articles were screened, of which 131 were excluded, and 78 were abstracted. No studies, outside of bisphosphonate trials, were identified that examined the impact of SREs as a group on clinical outcomes. In bisphosphonate trials, patients with SREs had significantly more pain and worse 1-year survival compared with no SREs. Pathologic bone fractures significantly decreased QOL and were associated with increased risk of death. Although spinal cord compression (SCC) has a significant impact on pain, improvement in morbidity may be achieved if SCC is treated. SCC is associated with significant decreases in patient survival. Radiation therapy improved pain and possibly QOL while bone surgery improved pain. Limited evidence suggested SREs increased cost by approximately €7,000 (Euros) and $12,000 (USD). **CONCLUSIONS:** Clinical SREs are associated with worse clinical outcomes, including pain, QOL, morbidity and survival, while treatment of clinical SREs is associated with improved pain and QOL among prostate cancer patients. SREs appear to increase cost substantially.

PCN22

SAFETY PROFILE OF BEVACIZUMAB IN METASTATIC COLORECTAL CANCER

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OBJECTIVES: To assess the overall risk of bevacizumab related adverse events in patients with metastatic colorectal cancer (mCRC). **METHODS:** A systematic review of the literature was conducted. The selection criteria of the studies for this review were: health technology agencies reports, meta-analysis, systematic reviews, randomized controlled trials (RCTs) and observational studies in patients treated with bevacizumab for mCRC. MEDLINE, EMBASE, the Cochrane Library, and CRD databases were searched until June 8, 2011. The selection of the studies, quality assessment, data extraction and data analysis were done independently by two authors. Disagreements were resolved by a third reviewer until consensus was obtained. **RESULTS:** To evaluate the safety profile of bevacizumab, two systematic reviews with meta-analysis and two observational studies were included (the BEAT and the BRiTE studies). A total of 3271 patients were included in one meta-analysis, which evaluated the risk of fatal adverse events (FAE) and 3,385 patients were included in the other meta-analysis, which evaluated any grade of toxicity. An increased risk of FAE was not observed between patients with mCRC receiving bevacizumab in combination with chemotherapy and patients receiving chemotherapy alone [Relative Risk (RR):1.21 Confidence Interval (CI) 95%: 0.65-2.24]. Patients treated with bevacizumab had an increased risk of developing grade 3-4 hypertension (RR: 4.27; CI95%: 2.80–6.51), any grade gastrointestinal perforation (RR: 5.04; CI95%: 1.72–14.79), grade 3-4 arterial thromboembolic events (RR: 1.23; CI95%: 0.93–1.62), and discontinuation because of grade 3-4 adverse events (RR: 1.21; CI95%: 1.03–1.43). The results from the observational studies were consistent with the data reported in the meta-analysis. **CONCLUSIONS:** Although the risk of FAE was not increased with bevacizumab in patients with mCRC, grade 3-4 hypertension, any grade gastrointestinal perforation, grade 3-4 arterial thromboembolic events, and discontinuation due to grade 3-4 adverse events were higher in the bevacizumab group.

PCN23

SURVIVAL ANALYSES ADJUSTED FOR CROSSOVER IN RELAPSED MULTIPLE MYELOMA: RESULTS OF THE APEX TRIAL

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OBJECTIVES: An interim analysis of APEX, a phase III randomized, open-label clinical trial, demonstrated superiority of bortezomib over high-dose dexamethasone in terms of time to disease progression (TTP). According to the original study protocol, patients were allowed to cross over on disease progression. Following interim analysis, patients could cross over regardless of the disease status. The ITT analysis of overall survival (OS) may therefore result in a biased estimate of the treatment effect. This study aimed to adjust the analysis for crossover. **METHODS:** The Iterative Parameter Estimation (IPE) algorithm using a Weibull distribution was selected as the primary analysis based on the findings from a simulation study (Morden et al). The IPE algorithm using a Gompertz distribution and the Rank